

# ANDROGEL- testosterone gel

## A-S Medication Solutions LLC

### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ANDROGEL 1.62% safely and effectively. See full prescribing information for ANDROGEL 1.62%.

AndroGel® (testosterone gel) 1.62% for topical use CIII

Initial U.S. Approval: 1953

#### WARNING: SECONDARY EXPOSURE TO TESTOSTERONE

- Virilization has been reported in children who were secondarily exposed to testosterone gel (5.2, 6.2).
- Children should avoid contact with unwashed or unclothed application sites in men using testosterone gel (2.2, 5.2).
- Healthcare providers should advise patients to strictly adhere to recommended instructions for use (2.2, 5.2, 17).

#### RECENT MAJOR CHANGES

Indications and Usage. (1) 09/2012

#### INDICATIONS AND USAGE

AndroGel 1.62% is an androgen indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired) (1)
- Hypogonadotropic hypogonadism (congenital or acquired) (1)

Important limitations of use:

- Safety and efficacy of AndroGel 1.62% in males less than 18 years old have not been established. (1, 8.4)
- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure. (1, 12.3)

#### DOSAGE AND ADMINISTRATION

- **Dosage and Administration for AndroGel 1.62% differs from AndroGel 1%. For dosage and administration of AndroGel 1% refer to its full prescribing information. (2)**
- Starting dose of AndroGel 1.62% is 40.5 mg of testosterone (2 pump actuations or a single 40.5 mg packet), applied topically once daily in the morning. (2.1)
- Apply to clean, dry, intact skin of the shoulders and upper arms. Do not apply AndroGel 1.62% to any other parts of the body including the abdomen or genitals. (2.2, 12.3)
- Dose adjustment: AndroGel 1.62% can be dose adjusted between a minimum of 20.25 mg of testosterone (1 pump actuation or a single 20.25 mg packet) and a maximum of 81 mg of testosterone (4 pump actuations or two 40.5 mg packets). The dose should be titrated based on the pre-dose morning serum testosterone concentration at approximately 14 days and 28 days after starting treatment or following dose adjustment. Additionally, serum testosterone concentration should be assessed periodically thereafter. (2.1)
- Patients should wash hands immediately with soap and water after applying AndroGel 1.62% and cover the application site(s) with clothing after the gel has dried. Wash the application site thoroughly with soap and water prior to any situation where skin-to-skin contact of the application site with another person is anticipated. (2.2)

#### DOSAGE FORMS AND STRENGTHS

AndroGel (testosterone gel) 1.62% for topical use is available as follows:

- a metered-dose pump that delivers 20.25 mg testosterone per actuation. (3)
- packets containing 20.25 mg testosterone. (3)
- packets containing 40.5 mg testosterone. (3)

#### CONTRAINDICATIONS

- Men with carcinoma of the breast or known or suspected prostate cancer (4, 5.1)
- Pregnant or breast-feeding women. Testosterone may cause fetal harm (4, 8.1, 8.3)

#### WARNINGS AND PRECAUTIONS

- Monitor patients with benign prostatic hyperplasia (BPH) for worsening of signs and symptoms of BPH (5.1)
- Avoid unintentional exposure of women or children to AndroGel 1.62%. Secondary exposure to testosterone can

- produce signs of virilization. AndroGel 1.62% should be discontinued until the cause of virilization is identified (5.2)
- Exogenous administration of androgens may lead to azoospermia (5.5)
- Edema with or without congestive heart failure (CHF) may be a complication in patients with preexisting cardiac, renal, or hepatic disease (5.7)
- Sleep apnea may occur in those with risk factors (5.9)
- Monitor serum testosterone, prostate specific antigen (PSA), hemoglobin, hematocrit, liver function tests and lipid concentrations periodically (5.1, 5.3, 5.6, 5.10)
- AndroGel 1.62% is flammable until dry (5.13)

#### ----- ADVERSE REACTIONS -----

The most common adverse reaction (incidence  $\geq 5\%$ ) is an increase in prostate specific antigen (PSA). (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Abbott Laboratories at 1-800-241-1643 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

#### ----- DRUG INTERACTIONS -----

- Androgens may decrease blood glucose and therefore may decrease insulin requirements in diabetic patients (7.1)
- Changes in anticoagulant activity may be seen with androgens. More frequent monitoring of International Normalized Ratio (INR) and prothrombin time is recommended (7.2)
- Use of testosterone with adrenocorticotrophic hormone (ACTH) or corticosteroids may result in increased fluid retention. Use with caution, particularly in patients with cardiac, renal, or hepatic disease (7.3)

#### ----- USE IN SPECIFIC POPULATIONS -----

There are insufficient long-term safety data in geriatric patients using AndroGel 1.62% to assess the potential risks of cardiovascular disease and prostate cancer. (8.5)

**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.**

**Revised: 3/2013**

## **FULL PRESCRIBING INFORMATION: CONTENTS\***

### **WARNING: SECONDARY EXPOSURE TO TESTOSTERONE**

#### **1 INDICATIONS AND USAGE**

#### **2 DOSAGE AND ADMINISTRATION**

##### 2.1 Dosing and Dose Adjustment

##### 2.2 Administration Instructions

#### **3 DOSAGE FORMS AND STRENGTHS**

#### **4 CONTRAINDICATIONS**

#### **5 WARNINGS AND PRECAUTIONS**

##### 5.1 Worsening of Benign Prostatic Hyperplasia (BPH) and Potential Risk of Prostate Cancer

##### 5.2 Potential for Secondary Exposure to Testosterone

##### 5.3 Polycythemia

##### 5.4 Use in Women

##### 5.5 Potential for Adverse Effects on Spermatogenesis

##### 5.6 Hepatic Adverse Effects

##### 5.7 Edema

##### 5.8 Gynecomastia

##### 5.9 Sleep Apnea

##### 5.10 Lipids

##### 5.11 Hypercalcemia

##### 5.12 Decreased Thyroxine-binding Globulin

##### 5.13 Flammability

#### **6 ADVERSE REACTIONS**

##### 6.1 Clinical Trial Experience

##### 6.2 Postmarketing Experience

#### **7 DRUG INTERACTIONS**

- 7.1 Insulin
- 7.2 Oral Anticoagulants
- 7.3 Corticosteroids

## **8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

## **9 DRUG ABUSE AND DEPENDENCE**

- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

## **10 OVERDOSAGE**

## **11 DESCRIPTION**

## **12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

## **13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

## **14 CLINICAL STUDIES**

- 14.1 Clinical Trials in Hypogonadal Males

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

## **17 PATIENT COUNSELING INFORMATION**

- 17.1 Use in Men with Known or Suspected Prostate or Breast Cancer
- 17.2 Potential for Secondary Exposure to Testosterone and Steps to Prevent Secondary Exposure
- 17.3 Potential Adverse Reactions with Androgens
- 17.4 Patients Should Be Advised of the Following Instructions for Use

\* Sections or subsections omitted from the full prescribing information are not listed.

---

## **FULL PRESCRIBING INFORMATION**

### **WARNING: SECONDARY EXPOSURE TO TESTOSTERONE**

- **Virilization has been reported in children who were secondarily exposed to testosterone gel [see Warnings and Precautions (5.2) and Adverse Reactions (6.2)].**
- **Children should avoid contact with unwashed or unclothed application sites in men using testosterone gel [see Dosage and Administration (2.2) and Warnings and Precautions (5.2)].**
- **Healthcare providers should advise patients to strictly adhere to recommended instructions for use [see Dosage and Administration (2.2), Warnings and Precautions (5.2) and Patient Counseling Information (17)].**

## **1 INDICATIONS AND USAGE**

AndroGel 1.62% is an androgen indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): idiopathic gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations, but have gonadotropins in the normal or low range.

Important limitations of use:

- Safety and efficacy of AndroGel 1.62% in males less than 18 years old have not been established [see *Use in Specific Populations* (8.4)].
- Topical testosterone products may have different doses, strengths, or application instructions that may result in different systemic exposure [see *Indications and Usage* (1), and *Clinical Pharmacology* (12.3)].

## 2 DOSAGE AND ADMINISTRATION

**Dosage and Administration for AndroGel 1.62% differs from AndroGel 1%. For dosage and administration of AndroGel 1% refer to its full prescribing information. (2)**

### 2.1 Dosing and Dose Adjustment

The recommended starting dose of AndroGel 1.62% is 40.5 mg of testosterone (2 pump actuations or a single 40.5 mg packet) applied topically once daily in the morning to the shoulders and upper arms.

The dose can be adjusted between a minimum of 20.25 mg of testosterone (1 pump actuation or a single 20.25 mg packet) and a maximum of 81 mg of testosterone (4 pump actuations or two 40.5 mg packets). To ensure proper dosing, the dose should be titrated based on the pre-dose morning serum testosterone concentration from a single blood draw at approximately 14 days and 28 days after starting treatment or following dose adjustment. In addition, serum testosterone concentration should be assessed periodically thereafter. Table 1 describes the dose adjustments required at each titration step.

**Table 1: Dose Adjustment Criteria**

<b>Pre-Dose Morning Total Serum Testosterone Concentration</b>	<b>Dose Titration</b>
Greater than 750 ng/dL	Decrease daily dose by 20.25 mg (1 pump actuation or the equivalent of one 20.25 mg packet)
Equal to or greater than 350 and equal to or less than 750 ng/dL	No change: continue on current dose
Less than 350 ng/dL	Increase daily dose by 20.25 mg (1 pump actuation or the equivalent of one 20.25 mg packet)

The application site and dose of AndroGel 1.62% are not interchangeable with other topical testosterone products.

### 2.2 Administration Instructions

AndroGel 1.62% should be applied to clean, dry, intact skin of the upper arms and shoulders. Do not apply AndroGel 1.62% to any other parts of the body, including the abdomen or genitals [see *Clinical Pharmacology* (12.3)]. Area of application should be limited to the area that will be covered by the patient's short sleeve t-shirt. Patients should be instructed to use the palm of the hand to apply AndroGel

1.62% and spread across the maximum surface area as directed in Table 2 (for pump) and Table 3 (for packets) and in Figure 1.

**Table 2: Application Sites for AndroGel 1.62%, Pump**

Total Dose of Testosterone	Total Pump Actuations	Pump Actuations Per Upper Arm and Shoulder	
		Upper Arm and Shoulder #1	Upper Arm and Shoulder #2
20.25 mg	1	1	0
40.5 mg	2	1	1
60.75 mg	3	2	1
81 mg	4	2	2

**Table 3: Application Sites for AndroGel 1.62%, Packets**

Total Dose of Testosterone	Total packets	Gel Applications Per Upper Arm and Shoulder	
		Upper Arm and Shoulder #1	Upper Arm and Shoulder #2
20.25 mg	One 20.25 mg packet	One 20.25 mg packet	0
40.5 mg	One 40.5 mg packet	Half of contents of One 40.5 mg packet	Half of contents of One 40.5 mg packet
60.75 mg	One 20.25 mg packet AND One 40.5 mg packet	One 40.5 mg packet	One 20.25 mg packet
81 mg	Two 40.5 mg packets	One 40.5 mg packet	One 40.5 mg packet

The prescribed daily dose of AndroGel 1.62% should be applied to the right and left upper arms and shoulders as shown in the shaded areas in Figure 1.



**Figure 1. Application Sites for AndroGel 1.62%**

Once the application site is dry, the site should be covered with clothing [see *Clinical Pharmacology* (12.3)]. Wash hands thoroughly with soap and water. Avoid fire, flames or smoking until the gel has dried since alcohol based products, including AndroGel 1.62%, are flammable.

The patient should avoid swimming or showering or washing the administration site for a minimum of 2 hours after application [see *Clinical Pharmacology* (12.3)].

To obtain a full first dose, it is necessary to prime the canister pump. To do so, with the canister in the upright position, slowly and fully depress the actuator three times. Safely discard the gel from the first three actuations. It is only necessary to prime the pump before the first dose.

After the priming procedure, fully depress the actuator once for every 20.25 mg of AndroGel 1.62%. AndroGel 1.62% should be delivered directly into the palm of the hand and then applied to the application sites.

When using packets, the entire contents should be squeezed into the palm of the hand and immediately applied to the application sites. When 40.5 mg packets need to be split between the left and right shoulder, patients may squeeze a portion of the gel from the packet into the palm of the hand and apply to application sites. Repeat until entire contents have been applied. Alternatively, AndroGel 1.62% can be applied directly to the application sites from the pump or packets.

**Strict adherence to the following precautions is advised in order to minimize the potential for secondary exposure to testosterone from AndroGel 1.62%-treated skin:**

- Children and women should avoid contact with unwashed or unclothed application site(s) of men using AndroGel 1.62%.
- AndroGel 1.62% should only be applied to the upper arms and shoulders. The area of application should be limited to the area that will be covered by a short sleeve t-shirt.
- Patients should wash their hands with soap and water immediately after applying AndroGel 1.62%.
- Patients should cover the application site(s) with clothing (e.g., a t-shirt) after the gel has dried.
- Prior to situations in which direct skin-to-skin contact is anticipated, patients should wash the application site(s) thoroughly with soap and water to remove any testosterone residue.
- In the event that unwashed or unclothed skin to which AndroGel 1.62% has been applied comes in direct contact with the skin of another person, the general area of contact on the other person should be washed with soap and water as soon as possible.

### **3 DOSAGE FORMS AND STRENGTHS**

AndroGel (testosterone gel) 1.62% for topical use only, is available as follows:

- A metered-dose pump. Each pump actuation delivers 20.25 mg of testosterone in 1.25 g of gel.
- A unit dose packet containing 20.25 mg of testosterone in 1.25 g of gel.
- A unit dose packet containing 40.5 mg of testosterone in 2.5 g of gel.

### **4 CONTRAINDICATIONS**

- AndroGel 1.62% is contraindicated in men with carcinoma of the breast or known or suspected carcinoma of the prostate [*see Warnings and Precautions (5.1) and Adverse Reactions (6.1)*].
- AndroGel 1.62% is contraindicated in women who are or may become pregnant, or who are breastfeeding. AndroGel 1.62% may cause fetal harm when administered to a pregnant woman. AndroGel 1.62% may cause serious adverse reactions in nursing infants. Exposure of a fetus or nursing infant to androgens may result in varying degrees of virilization. Pregnant women or those who may become pregnant need to be aware of the potential for transfer of testosterone from men treated with AndroGel 1.62%. If a pregnant woman is exposed to AndroGel 1.62%, she should be apprised of the potential hazard to the fetus [*see Warnings and Precautions (5.2) and Use in Specific Populations (8.1, 8.3)*].

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Worsening of Benign Prostatic Hyperplasia (BPH) and Potential Risk of Prostate Cancer**

- Patients with BPH treated with androgens are at an increased risk for worsening of signs and symptoms of BPH. Monitor patients with BPH for worsening signs and symptoms.
- Patients treated with androgens may be at increased risk for prostate cancer. Evaluation of patients for prostate cancer prior to initiating and during treatment with androgens is appropriate [*see Contraindications (4)*].

## **5.2 Potential for Secondary Exposure to Testosterone**

Cases of secondary exposure resulting in virilization of children have been reported in postmarketing surveillance of testosterone gel products. Signs and symptoms have included enlargement of the penis or clitoris, development of pubic hair, increased erections and libido, aggressive behavior, and advanced bone age. In most cases, these signs and symptoms regressed with removal of the exposure to testosterone gel. In a few cases, however, enlarged genitalia did not fully return to age-appropriate normal size, and bone age remained modestly greater than chronological age. The risk of transfer was increased in some of these cases by not adhering to precautions for the appropriate use of the topical testosterone product. Children and women should avoid contact with unwashed or unclothed application sites in men using AndroGel 1.62% [*see Dosage and Administration (2.2), Use in Specific Populations (8.1) and Clinical Pharmacology (12.3)*].

Inappropriate changes in genital size or development of pubic hair or libido in children, or changes in body hair distribution, significant increase in acne, or other signs of virilization in adult women should be brought to the attention of a physician and the possibility of secondary exposure to testosterone gel should also be brought to the attention of a physician. Testosterone gel should be promptly discontinued until the cause of virilization has been identified.

## **5.3 Polycythemia**

Increases in hematocrit, reflective of increases in red blood cell mass, may require lowering or discontinuation of testosterone. Check hematocrit prior to initiating treatment. It would also be appropriate to re-evaluate the hematocrit 3 to 6 months after starting treatment, and then annually. If hematocrit becomes elevated, stop therapy until hematocrit decreases to an acceptable concentration. An increase in red blood cell mass may increase the risk of thromboembolic events.

## **5.4 Use in Women**

Due to the lack of controlled evaluations in women and potential virilizing effects, AndroGel 1.62% is not indicated for use in women [*see Contraindications (4) and Use in Specific Populations (8.1, 8.3)*].

## **5.5 Potential for Adverse Effects on Spermatogenesis**

With large doses of exogenous androgens, including AndroGel 1.62%, spermatogenesis may be suppressed through feedback inhibition of pituitary FSH possibly leading to adverse effects on semen parameters including sperm count.

## **5.6 Hepatic Adverse Effects**

Prolonged use of high doses of orally active 17-alpha-alkyl androgens (e.g., methyltestosterone) has been associated with serious hepatic adverse effects (peliosis hepatis, hepatic neoplasms, cholestatic hepatitis, and jaundice). Peliosis hepatis can be a life-threatening or fatal complication. Long-term therapy with intramuscular testosterone enanthate has produced multiple hepatic adenomas. AndroGel 1.62% is not known to cause these adverse effects.

## **5.7 Edema**

Androgens, including AndroGel 1.62%, may promote retention of sodium and water. Edema, with or without congestive heart failure, may be a serious complication in patients with preexisting cardiac, renal, or hepatic disease [*see Adverse Reactions (6.2)*].

## **5.8 Gynecomastia**

Gynecomastia may develop and persist in patients being treated with androgens, including AndroGel 1.62%, for hypogonadism.

## **5.9 Sleep Apnea**

The treatment of hypogonadal men with testosterone may potentiate sleep apnea in some patients, especially those with risk factors such as obesity or chronic lung diseases.

### 5.10 Lipids

Changes in serum lipid profile may require dose adjustment or discontinuation of testosterone therapy.

### 5.11 Hypercalcemia

Androgens, including AndroGel 1.62 %, should be used with caution in cancer patients at risk of hypercalcemia (and associated hypercalciuria). Regular monitoring of serum calcium concentrations is recommended in these patients.

### 5.12 Decreased Thyroxine-binding Globulin

Androgens, including AndroGel 1.62%, may decrease concentrations of thyroxin-binding globulins, resulting in decreased total T4 serum concentrations and increased resin uptake of T3 and T4. Free thyroid hormone concentrations remain unchanged, however, and there is no clinical evidence of thyroid dysfunction.

### 5.13 Flammability

**Alcohol based products, including AndroGel 1.62%, are flammable; therefore, patients should be advised to avoid fire, flame or smoking until the AndroGel 1.62% has dried.**

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

AndroGel 1.62% was evaluated in a two-phase, 364-day, controlled clinical study. The first phase was a multi-center, randomized, double-blind, parallel-group, placebo-controlled period of 182 days, in which 234 hypogonadal men were treated with AndroGel 1.62% and 40 received placebo. Patients could continue in an open-label, non-comparative, maintenance period for an additional 182 days [see *Clinical Studies (14.1)*].

The most common adverse reaction reported in the double-blind period was increased prostate specific antigen (PSA) reported in 26 AndroGel 1.62%-treated patients (11.1%). In 17 patients, increased PSA was considered an adverse event by meeting one of the two pre-specified criteria for abnormal PSA values, defined as (1) average serum PSA >4 ng/mL based on two separate determinations, or (2) an average change from baseline in serum PSA of greater than 0.75 ng/mL on two determinations.

During the 182-day, double-blind period of the clinical trial, the mean change in serum PSA value was 0.14 ng/mL for patients receiving AndroGel 1.62% and -0.12 ng/mL for the patients in the placebo group. During the double-blind period, seven patients had a PSA value >4.0 ng/mL, four of these seven patients had PSA less than or equal to 4.0 ng/mL upon repeat testing. The other three patients did not undergo repeat PSA testing.

During the 182-day, open-label period of the study, the mean change in serum PSA values was 0.10 ng/mL for both patients continuing on active therapy and patients transitioning onto active from placebo. During the open-label period, three patients had a serum PSA value > 4.0 ng/mL, two of whom had a serum PSA less than or equal to 4.0 ng/mL upon repeated testing. The other patient did not undergo repeat PSA testing. Among previous placebo patients, 3 of 28 (10.7%), had increased PSA as an adverse event in the open-label period.

Table 4 shows adverse reactions reported by >2% of patients in the 182-day, double-blind period of the



AndroGel 1.62% clinical trial and more frequent in the AndroGel 1.62% treated group versus placebo.

**Table 4: Adverse Reactions Reported in >2% of Patients in the 182-Day, Double-Blind Period of AndroGel 1.62% Clinical Trial**

Adverse Reaction	Number (%) of Patients	
	AndroGel 1.62% N=234	Placebo N= 40
PSA increased*	26 (11.1%)	0%
Emotional lability**	6 (2.6%)	0%
Hypertension	5 (2.1%)	0%
Hematocrit or hemoglobin increased	5 (2.1%)	0%
Contact dermatitis***	5 (2.1%)	0%

\***PSA increased** includes: PSA values that met pre-specified criteria for abnormal PSA values (an average change from baseline > 0.75 ng/mL and/or an average PSA value >4.0 ng/mL based on two measurements) as well as those reported as adverse events.

\*\***Emotional lability** includes: mood swings, affective disorder, impatience, anger, and aggression.

\*\*\***Contact dermatitis** includes: 4 patients with dermatitis at non-application sites.

Other adverse reactions occurring in less than or equal to 2% of AndroGel 1.62%-treated patients and more frequently than placebo included: frequent urination, and hyperlipidemia.

In the open-label period of the study (N=191), the most commonly reported adverse reaction (experienced by greater than 2% of patients) was increased PSA (n=13; 6.2%) and sinusitis. Other adverse reactions reported by less than or equal to 2% of patients included increased hemoglobin or hematocrit, hypertension, acne, libido decreased, insomnia, and benign prostatic hypertrophy.

During the 182-day, double-blind period of the clinical trial, 25 AndroGel 1.62%-treated patients (10.7%) discontinued treatment because of adverse reactions. These adverse reactions included 17 patients with PSA increased and 1 report each of: hematocrit increased, blood pressure increased, frequent urination, diarrhea, fatigue, pituitary tumor, dizziness, skin erythema and skin nodule (same patient – neither at application site), vasovagal syncope, and diabetes mellitus. During the 182-day, open-label period, 9 patients discontinued treatment because of adverse reactions. These adverse reactions included 6 reports of PSA increased, 2 of hematocrit increased, and 1 each of triglycerides increased and prostate cancer.

### Application Site Reactions

In the 182-day double-blind period of the study, application site reactions were reported in two (2/234; 0.9%) patients receiving AndroGel 1.62%, both of which resolved. Neither of these patients discontinued the study due to application site adverse reactions. In the open-label period of the study, application site reactions were reported in three (3/219; 1.4%) additional patients that were treated with AndroGel 1.62%. None of these subjects were discontinued from the study due to application site reactions.

## 6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of AndroGel 1%. Because the reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure (Table 5).

**Table 5: Adverse Reactions from Post Approval Experience of AndroGel 1% by System Organ Class**

System Organ Class	Adverse Reaction
<b>Blood and lymphatic system disorders:</b>	Elevated hemoglobin or hematocrit, polycythemia, anemia
<b>Endocrine disorders:</b>	Hirsutism
<b>Gastrointestinal disorders:</b>	Nausea
<b>General disorders:</b>	Asthenia, edema, malaise
<b>Genitourinary disorders:</b>	Impaired urination*
<b>Hepatobiliary disorders:</b>	Abnormal liver function tests
<b>Investigations:</b>	Lab test abnormal**, elevated PSA, electrolyte changes (nitrogen, calcium, potassium [includes hypokalemia], phosphorus, sodium), impaired glucose tolerance, hyperlipidemia, HDL, fluctuating testosterone levels, weight increase
<b>Neoplasms:</b>	Prostate cancer
<b>Nervous system disorders:</b>	Dizziness, headache, insomnia, sleep apnea
<b>Psychiatric disorders:</b>	Amnesia, anxiety, depression, hostility, emotional lability, decreased libido, nervousness
<b>Reproductive system and breast disorders:</b>	Gynecomastia, mastodynia, oligospermia, priapism (frequent or prolonged erections), prostate enlargement, BPH, testis disorder***
<b>Respiratory disorders:</b>	Dyspnea
<b>Skin and subcutaneous tissue disorders:</b>	Acne, alopecia, application site reaction (discolored hair, dry skin, erythema, paresthesia, pruritus, rash), skin dry, pruritus, sweating
<b>Vascular disorders:</b>	Hypertension, vasodilation (hot flushes)

\* **Impaired urination includes** nocturia, urinary hesitancy, urinary incontinence, urinary retention, urinary urgency and weak urinary stream

\*\***Lab test abnormal includes** elevated AST, elevated ALT, elevated testosterone, elevated hemoglobin or hematocrit, elevated cholesterol, elevated cholesterol/LDL ratio, elevated triglycerides, or elevated serum creatinine

\*\*\***Testis disorder includes** atrophy or non-palpable testis, varicocele, testis sensitivity or tenderness

### Secondary Exposure to Testosterone in Children

Cases of secondary exposure to testosterone resulting in virilization of children have been reported in postmarketing surveillance of testosterone gel products. Signs and symptoms of these reported cases have included enlargement of the clitoris (with surgical intervention) or the penis, development of pubic hair, increased erections and libido, aggressive behavior, and advanced bone age. In most cases with a reported outcome, these signs and symptoms were reported to have regressed with removal of the testosterone gel exposure. In a few cases, however, enlarged genitalia did not fully return to age appropriate normal size, and bone age remained modestly greater than chronological age. In some of the cases, direct contact with the sites of application on the skin of men using testosterone gel was reported. In at least one reported case, the reporter considered the possibility of secondary exposure from items such as the testosterone gel user's shirts and/or other fabric, such as towels and sheets [see *Warnings and Precautions* (5.2)].

## 7 DRUG INTERACTIONS

### 7.1 Insulin

Changes in insulin sensitivity or glycemic control may occur in patients treated with androgens. In diabetic patients, the metabolic effects of androgens may decrease blood glucose and, therefore, may

decrease insulin requirements.

## **7.2 Oral Anticoagulants**

Changes in anticoagulant activity may be seen with androgens, therefore more frequent monitoring of international normalized ratio (INR) and prothrombin time are recommended in patients taking anticoagulants, especially at the initiation and termination of androgen therapy.

## **7.3 Corticosteroids**

The concurrent use of testosterone with adrenocorticotrophic hormone (ACTH) or corticosteroids may result in increased fluid retention and requires careful monitoring particularly in patients with cardiac, renal or hepatic disease.

# **8 USE IN SPECIFIC POPULATIONS**

## **8.1 Pregnancy**

Pregnancy Category X [*see Contraindications (4)*]: AndroGel 1.62% is contraindicated during pregnancy or in women who may become pregnant. Testosterone is teratogenic and may cause fetal harm. Exposure of a fetus to androgens may result in varying degrees of virilization. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be made aware of the potential hazard to the fetus.

## **8.3 Nursing Mothers**

Although it is not known how much testosterone transfers into human milk, AndroGel 1.62% is contraindicated in nursing women because of the potential for serious adverse reactions in nursing infants. Testosterone and other androgens may adversely affect lactation [*see Contraindications (4)*].

## **8.4 Pediatric Use**

The safety and effectiveness of AndroGel 1.62% in pediatric patients less than 18 years old has not been established. Improper use may result in acceleration of bone age and premature closure of epiphyses.

## **8.5 Geriatric Use**

There have not been sufficient numbers of geriatric patients involved in controlled clinical studies utilizing AndroGel 1.62% to determine whether efficacy in those over 65 years of age differs from younger subjects. Of the 234 patients enrolled in the clinical trial utilizing AndroGel 1.62%, 21 were over 65 years of age. Additionally, there is insufficient long-term safety data in geriatric patients to assess the potentially increased risks of cardiovascular disease and prostate cancer.

Geriatric patients treated with androgens may also be at risk for worsening of signs and symptoms of BPH.

## **8.6 Renal Impairment**

No studies were conducted involving patients with renal impairment.

## **8.7 Hepatic Impairment**

No studies were conducted in patients with hepatic impairment.

# **9 DRUG ABUSE AND DEPENDENCE**

## **9.1 Controlled Substance**

AndroGel 1.62% contains testosterone, a Schedule III controlled substance in the Controlled Substances Act.

## 9.2 Abuse

Anabolic steroids, such as testosterone, are abused. Abuse is often associated with adverse physical and psychological effects.

## 9.3 Dependence

Although drug dependence is not documented in individuals using therapeutic doses of anabolic steroids for approved indications, dependence is observed in some individuals abusing high doses of anabolic steroids. In general, anabolic steroid dependence is characterized by any three of the following:

- Taking more drug than intended
- Continued drug use despite medical and social problems
- Significant time spent in obtaining adequate amounts of drug
- Desire for anabolic steroids when supplies of the drugs are interrupted
- Difficulty in discontinuing use of the drug despite desires and attempts to do so
- Experience of a withdrawal syndrome upon discontinuation of anabolic steroid use

## 10 OVERDOSAGE

There is a single report of acute overdosage after parenteral administration of an approved testosterone product in the literature. This subject had serum testosterone concentrations of up to 11,400 ng/dL, which were implicated in a cerebrovascular accident. There were no reports of overdosage in the AndroGel 1.62% clinical trial.

Treatment of overdosage would consist of discontinuation of AndroGel 1.62%, washing the application site with soap and water, and appropriate symptomatic and supportive care.

## 11 DESCRIPTION

AndroGel 1.62% for topical use is a clear, colorless gel containing testosterone. Testosterone is an androgen. AndroGel 1.62% is available in a metered-dose pump or unit dose packets.

The active pharmacologic ingredient in AndroGel 1.62% is testosterone. Testosterone USP is a white to almost white powder chemically described as 17-beta hydroxyandrost-4-en-3-one. The structural formula is:



The inactive ingredients in AndroGel 1.62% are: carbopol 980, ethyl alcohol, isopropyl myristate, purified water, and sodium hydroxide.

## 12 CLINICAL PHARMACOLOGY

## 12.1 Mechanism of Action

Endogenous androgens, including testosterone and dihydrotestosterone (DHT), are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. These effects include the growth and maturation of prostate, seminal vesicles, penis and scrotum; the development of male hair distribution, such as facial, pubic, chest and axillary hair; laryngeal enlargement; vocal chord thickening; and alterations in body musculature and fat distribution. Testosterone and DHT are necessary for the normal development of secondary sex characteristics. Male hypogonadism results from insufficient secretion of testosterone and is characterized by low serum testosterone concentrations. Signs/symptoms associated with male hypogonadism include erectile dysfunction and decreased sexual desire, fatigue and loss of energy, mood depression, regression of secondary sexual characteristics and osteoporosis.

Male hypogonadism can present as primary hypogonadism caused by defects of the gonads, such as Klinefelter's Syndrome or Leydig cell aplasia while secondary hypogonadism is the failure of the hypothalamus or pituitary to produce sufficient gonadotropins (FSH, LH).

## 12.2 Pharmacodynamics

No specific pharmacodynamic studies were conducted using AndroGel 1.62%.

## 12.3 Pharmacokinetics

### ***Absorption***

AndroGel 1.62% delivers physiologic amounts of testosterone, producing circulating testosterone concentrations that approximate normal levels (300 – 1000 ng/dL) seen in healthy men. AndroGel 1.62% provides continuous transdermal delivery of testosterone for 24 hours following once daily application to clean, dry, intact skin of the shoulders and upper arms. Average serum testosterone concentrations over 24 hours ( $C_{avg}$ ) observed when AndroGel 1.62% was applied to the upper arms/shoulders were comparable to average serum testosterone concentrations ( $C_{avg}$ ) when AndroGel 1.62% was applied using a rotation method utilizing the abdomen and upper arms/shoulders. The rotation of abdomen and upper arms/shoulders was a method used in the pivotal clinical trial [see *Clinical Studies (14.1)*].

**Figure 2: Mean ( $\pm$ SD) Serum Total Testosterone Concentrations on Day 7 in Patients Following AndroGel 1.62% Once-Daily Application of 81 mg of Testosterone (N=33) for 7 Days**

## ***Distribution***

Circulating testosterone is primarily bound in the serum to sex hormone-binding globulin (SHBG) and albumin. Approximately 40% of testosterone in plasma is bound to SHBG, 2% remains unbound (free) and the rest is loosely bound to albumin and other proteins.

## ***Metabolism***

Testosterone is metabolized to various 17-keto steroids through two different pathways. The major active metabolites of testosterone are estradiol and DHT.

## ***Excretion***

There is considerable variation in the half-life of testosterone concentration as reported in the literature, ranging from 10 to 100 minutes. About 90% of a dose of testosterone given intramuscularly is excreted in the urine as glucuronic acid and sulfuric acid conjugates of testosterone and its metabolites. About 6% of a dose is excreted in the feces, mostly in the unconjugated form. Inactivation of testosterone occurs primarily in the liver.

When AndroGel 1.62% treatment is discontinued, serum testosterone concentrations return to approximately baseline concentrations within 48-72 hours after administration of the last dose.

## ***Potential for testosterone transfer***

The potential for testosterone transfer following administration of AndroGel 1.62% when it was applied only to upper arms/shoulders was evaluated in two clinical studies of males dosed with AndroGel 1.62% and their untreated female partners. In one study, 8 male subjects applied a single dose of AndroGel 1.62% 81 mg to their shoulders and upper arms. Two (2) hours after application, female subjects rubbed their hands, wrists, arms, and shoulders to the application site of the male subjects for 15 minutes. Serum concentrations of testosterone were monitored in female subjects for 24 hours after contact occurred. After direct skin-to-skin contact with the site of application, mean testosterone  $C_{avg}$  and  $C_{max}$  in female subjects increased by 280% and 267%, respectively, compared to mean baseline testosterone concentrations. In a second study evaluating transfer of testosterone, 12 male subjects applied a single dose of AndroGel 1.62% 81 mg to their shoulders and upper arms. Two (2) hours after application, female subjects rubbed their hands, wrists, arms, and shoulders to the application site of the male subjects for 15 minutes while the site of application was covered by a t-shirt. When a t-shirt was used to cover the site of application, mean testosterone  $C_{avg}$  and  $C_{max}$  in female subjects increased by 6% and 11%, respectively, compared to mean baseline testosterone concentrations.

A separate study was conducted to evaluate the potential for testosterone transfer from 16 males dosed with AndroGel 1.62% 81 mg when it was applied to abdomen only for 7 days, a site of application not approved for AndroGel 1.62%. Two (2) hours after application to the males on each day, the female subjects rubbed their abdomens for 15 minutes to the abdomen of the males. The males had covered the application area with a T-shirt. The mean testosterone  $C_{avg}$  and  $C_{max}$  in female subjects on day 1 increased by 43% and 47%, respectively, compared to mean baseline testosterone concentrations. The mean testosterone  $C_{avg}$  and  $C_{max}$  in female subjects on day 7 increased by 60% and 58%, respectively, compared to mean baseline testosterone concentrations.

## ***Effect of showering***

In a randomized, 3-way (3 treatment periods without washout period) crossover study in 24 hypogonadal men, the effect of showering on testosterone exposure was assessed after once daily application of AndroGel 1.62% 81 mg to upper arms/shoulders for 7 days in each treatment period. On the 7th day of each treatment period, hypogonadal men took a shower with soap and water at either 2, 6, or 10 hours after drug application. The effect of showering at 2 or 6 hours post-dose on Day 7 resulted in 13% and 12% decreases in mean  $C_{avg}$ , respectively, compared to Day 6 when no shower was taken after drug application. Showering at 10 hours after drug application had no effect on bioavailability. The amount of testosterone remaining in the outer layers of the skin at the application site on the 7th day was

assessed using a tape stripping procedure and was reduced by at least 80% after showering 2-10 hours post-dose compared to on the 6th day when no shower was taken after drug application.

#### *Effect of sunscreen or moisturizing lotion on absorption of testosterone*

In a randomized, 3-way (3 treatment periods without washout period) crossover study in 18 hypogonadal males, the effect of applying a moisturizing lotion or a sunscreen on the absorption of testosterone was evaluated with the upper arms/shoulders as application sites. For 7 days, moisturizing lotion or sunscreen (SPF 50) was applied daily to the AndroGel 1.62% application site 1 hour after the application of AndroGel 1.62% 40.5 mg. Application of moisturizing lotion increased mean testosterone  $C_{avg}$  and  $C_{max}$  by 14% and 17%, respectively, compared to AndroGel 1.62% administered alone. Application of sunscreen increased mean testosterone  $C_{avg}$  and  $C_{max}$  by 8% and 13%, respectively, compared to AndroGel 1.62% applied alone.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Testosterone has been tested by subcutaneous injection and implantation in mice and rats. In mice, the implant induced cervical-uterine tumors which metastasized in some cases. There is suggestive evidence that injection of testosterone into some strains of female mice increases their susceptibility to hepatoma. Testosterone is also known to increase the number of tumors and decrease the degree of differentiation of chemically induced carcinomas of the liver in rats. Testosterone was negative in the *in vitro* Ames and in the *in vivo* mouse micronucleus assays. The administration of exogenous testosterone has been reported to suppress spermatogenesis in the rat, dog and non-human primates, which was reversible on cessation of the treatment.

## **14 CLINICAL STUDIES**

### **14.1 Clinical Trials in Hypogonadal Males**

AndroGel 1.62% was evaluated in a multi-center, randomized, double-blind, parallel-group, placebo-controlled study (182-day double-blind period) in 274 hypogonadal men with body mass index (BMI) 18-40 kg/m<sup>2</sup> and 18-80 years of age (mean age 53.8 years). The patients had an average serum testosterone concentration of <300 ng/dL, as determined by two morning samples collected on the same visit. Patients were Caucasian 83%, Black 13%, Asian or Native American 4%. 7.5% of patients were Hispanic.

Patients were randomized to receive active treatment or placebo using a rotation method utilizing the abdomen and upper arms/shoulders for 182 days. All patients were started at a daily dose of 40.5 mg (two pump actuations) AndroGel 1.62% or matching placebo on Day 1 of the study. Patients returned to the clinic on Day 14, Day 28, and Day 42 for predose serum total testosterone assessments. The patient's daily dose was titrated up or down in 20.25 mg increments if the predose serum testosterone value was outside the range of 350-750 ng/dL. The study included four active AndroGel 1.62% doses: 20.25 mg, 40.5 mg, 60.75 mg, and 81 mg daily.

The primary endpoint was the percentage of patients with  $C_{avg}$  within the normal range of 300-1000 ng/dL on Day 112. In patients treated with AndroGel 1.62%, 81.6% (146/179) had  $C_{avg}$  within the normal range at Day 112. The secondary endpoint was the percentage of patients, with  $C_{max}$  above three pre-determined limits. The percentages of patients with  $C_{max}$  greater than 1500 ng/dL, and between 1800 and 2499 ng/dL on Day 112 were 11.2% and 5.5%, respectively. Two patients had a  $C_{max}$  >2500 ng/dL on Day 112 (2510 ng/dL and 2550 ng/dL, respectively); neither of these 2 patients demonstrated an abnormal  $C_{max}$  on prior or subsequent assessments at the same dose.

Patients could agree to continue in an open-label, active treatment maintenance period of the study for an additional 182 days.

Dose titrations on Days 14, 28, and 42 resulted in final doses of 20.25 mg – 81 mg on Day 112 as shown in Table 6.

**Table 6: Mean (SD) Testosterone Concentrations ( $C_{avg}$  and  $C_{max}$ ) by final dose on Days 112 and 364**

Parameter	Final Dose on Day 112					
	Placebo (n=27)	20.25 mg (n=12)	40.5 mg (n=34)	60.75 mg (n=54)	81 mg (n=79)	
$C_{avg}$ (ng/dL)	303 (135)	457 (275)	524 (228)	643 (285)	537 (240)	561 (259)
$C_{max}$ (ng/dL)	450 (349)	663 (473)	798 (439)	958 (497)	813 (479)	845 (480)
Final Dose on Day 364						
		20.25 mg (n=7)	40.5 mg (n=26)	60.75 mg (n=29)	81 mg (n=74)	Continuing Active (n=136)
$C_{avg}$ (ng/dL)		386 (130)	474 (176)	513 (222)	432 (186)	455 (192)
$C_{max}$ (ng/dL)		562 (187)	715 (306)	839 (568)	649 (329)	697 (389)

Figure 3 summarizes the pharmacokinetic profile of total testosterone in patients completing 112 days of AndroGel 1.62% treatment administered as a starting dose of 40.5 mg of testosterone (2 pump actuations) for the initial 14 days followed by possible titration according to the follow-up testosterone measurements.

**Figure 3: Mean ( $\pm$ SD) Steady-State Serum Total Testosterone Concentrations on Day 112**

Efficacy was maintained in the group of men that received AndroGel 1.62% for one full year. In that group, 78% (106/136) had average serum testosterone concentrations in the normal range at Day 364. Figure 4 summarizes the mean total testosterone profile for these patients on Day 364.



**Figure 4: Mean ( $\pm$ SD) Steady-State Serum Total Testosterone Concentrations on Day 364**

The mean estradiol and DHT concentration profiles paralleled the changes observed in testosterone. The levels of LH and FSH decreased with testosterone treatment. The decreases in levels of LH and FSH are consistent with reports published in the literature of long-term treatment with testosterone.

**16 HOW SUPPLIED/STORAGE AND HANDLING**

AndroGel 1.62% is supplied in non-aerosol, metered-dose pumps that deliver 20.25 mg of testosterone per complete pump actuation. The pumps are composed of plastic and stainless steel and an LDPE/aluminum foil inner liner encased in rigid plastic with a polypropylene cap. Each 88 g metered-dose pump is capable of dispensing 75 g of gel or 60-metered pump actuations; each pump actuation dispenses 1.25 g of gel.

AndroGel 1.62% is also supplied in unit-dose aluminum foil packets in cartons of 30. Each packet of 1.25 g or 2.5 g gel contains 20.25 mg or 40.5 mg testosterone, respectively.

<b>NDC Number</b>	<b>Package Size</b>
0051-8462-33	88 g pump (each pump dispenses 60 metered pump actuations with each pump actuation containing 20.25 mg of testosterone in 1.25 g of gel)
0051-8462-12	Each unit dose packet contains 20.25 mg of testosterone provided in 1.25 g of gel
0051-8462-31	30 packets (each unit dose packet contains 20.25 mg of testosterone provided in 1.25 g of gel)
0051-8462-01	Each unit dose packet contains 40.5 mg of testosterone provided in 2.5 g of gel
0051-8462-30	30 packets (each unit dose packet contains 40.5 mg of testosterone provided in 2.5 g of gel)

Store at controlled room temperature 20°-25°C (68°-77°F); excursions permitted to 15°- 30°C (59°- 86°F) [see USP Controlled Room Temperature].

Used AndroGel 1.62% pumps or used AndroGel 1.62% packets should be discarded in household trash in a manner that prevents accidental application or ingestion by children or pets.

## 17 PATIENT COUNSELING INFORMATION

### See FDA-Approved Medication Guide

Patients should be informed of the following:

#### 17.1 Use in Men with Known or Suspected Prostate or Breast Cancer

Men with known or suspected prostate or breast cancer should not use AndroGel 1.62% [see *Contraindications (4) and Warnings and Precautions (5.1)*].

#### 17.2 Potential for Secondary Exposure to Testosterone and Steps to Prevent Secondary Exposure

Secondary exposure to testosterone in children and women can occur with the use of testosterone gel in men. Cases of secondary exposure to testosterone have been reported in children.

Physicians should advise patients of the reported signs and symptoms of secondary exposure, which may include the following:

- In children: unexpected sexual development including inappropriate enlargement of the penis or clitoris, premature development of pubic hair, increased erections, and aggressive behavior.
- In women: changes in hair distribution, increase in acne, or other signs of testosterone effects.
- The possibility of secondary exposure to testosterone gel should be brought to the attention of a healthcare provider.
- AndroGel 1.62% should be promptly discontinued until the cause of virilization is identified.

Strict adherence to the following precautions is advised to minimize the potential for secondary exposure to testosterone from AndroGel 1.62% in men [see *Medication Guide*]:

- **Children and women should avoid contact with unwashed or unclothed application site(s)** of men using AndroGel 1.62%.
- Patients using AndroGel 1.62% should apply the product as directed and strictly adhere to the following:
  - **Wash hands** with soap and water immediately after application.
  - **Cover the application site(s)** with clothing after the gel has dried.
  - **Wash the application site(s) thoroughly** with soap and water prior to any situation where skin-to-skin contact of the application site with another person is anticipated.
- In the event that unwashed or unclothed skin to which AndroGel 1.62% has been applied comes in contact with the skin of another person, the general area of contact on the other person should be washed with soap and water as soon as possible [see *Dosage and Administration (2.2)*, *Warnings and Precautions (5.2)* and *Clinical Pharmacology (12.3)*].

#### 17.3 Potential Adverse Reactions with Androgens

Patients should be informed that treatment with androgens may lead to adverse reactions which include:

- Changes in urinary habits such as increased urination at night, trouble starting the urine stream, passing urine many times during the day, having an urge to go to the bathroom right away, having a urine accident, being unable to pass urine and weak urine flow.
- Breathing disturbances, including those associated with sleep, or excessive daytime sleepiness.
- Too frequent or persistent erections of the penis.
- Nausea, vomiting, changes in skin color, or ankle swelling.

#### **17.4 Patients Should Be Advised of the Following Instructions for Use**

- **Read the Medication Guide before starting AndroGel 1.62% therapy and to reread it each time the prescription is renewed.**
- **AndroGel 1.62% should be applied and used appropriately to maximize the benefits and to minimize the risk of secondary exposure in children and women.**
- Keep AndroGel 1.62% out of the reach of children.
- **AndroGel 1.62% is an alcohol based product and is flammable; therefore avoid fire, flame or smoking until the gel has dried.**
- It is important to adhere to all recommended monitoring.
- Report any changes in their state of health, such as changes in urinary habits, breathing, sleep, and mood.
- AndroGel 1.62% is prescribed to meet the patient's specific needs; therefore, the patient should never share AndroGel 1.62% with anyone.
- Wait 2 hours before swimming or washing following application of AndroGel 1.62%. This will ensure that the greatest amount of AndroGel 1.62% is absorbed into their system.

A090630053786 September 2012

Marketed by:

Abbott Laboratories

North Chicago, IL, 60064, U.S.A.

© 2012 Abbott Laboratories

#### **Medication Guide**

#### **ANDROGEL® (AN DROW JEL) CIII**

#### **(testosterone gel) 1.62%**

Read this Medication Guide before you start using ANDROGEL 1.62% and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

#### **What is the most important information I should know about ANDROGEL 1.62%?**

1. **Early signs and symptoms of puberty have happened in young children who were accidentally exposed to testosterone through contact with men using ANDROGEL 1.62%.**

#### **Signs and symptoms of early puberty in a child may include:**

- enlarged penis or clitoris
- early development of pubic hair
- increased erections or sex drive
- aggressive behavior

#### **ANDROGEL 1.62% can transfer from your body to others.**

2. **Women and children should avoid contact with the unwashed or unclothed area where ANDROGEL 1.62% has been applied to your skin.**

**Stop using ANDROGEL 1.62% and call your healthcare provider right away if you see any signs and symptoms in a child or a woman that may have occurred through accidental exposure to ANDROGEL 1.62%.**

#### **Signs and symptoms of exposure to ANDROGEL 1.62% in children may include:**

- enlarged penis or clitoris
- early development of pubic hair

- increased erections or sex drive
- aggressive behavior

**Signs and symptoms of exposure to ANDROGEL 1.62% in women may include:**

- changes in body hair
- a large increase in acne
- **To lower the risk of transfer of ANDROGEL 1.62% from your body to others, you should follow these important instructions:**
  - Apply ANDROGEL 1.62% **only** to your shoulders and upper arms that will be covered by a short sleeve t-shirt.
  - Wash your hands **right away** with soap and water after applying ANDROGEL 1.62%.
  - After the gel has dried, **cover the application area with clothing**. Keep the area covered until you have washed the application area well or have showered.
  - **If you expect to have skin-to-skin contact with another person, first wash the application area well with soap and water.**
  - **If a woman or child makes contact with the ANDROGEL 1.62% application area, that area on the woman or child should be washed well with soap and water right away.**

**What is ANDROGEL 1.62%?**

ANDROGEL 1.62% is a prescription medicine that contains testosterone. ANDROGEL 1.62% is used to treat adult males who have low or no testosterone.

Your healthcare provider will test your blood before you start and while you are taking ANDROGEL 1.62%.

It is not known if ANDROGEL 1.62% is safe or effective in children younger than 18 years old. Improper use of ANDROGEL 1.62% may affect bone growth in children.

ANDROGEL 1.62% is a controlled substance (CIII) because it contains testosterone that can be a target for people who abuse prescription medicines. Keep your ANDROGEL 1.62% in a safe place to protect it. Never give your ANDROGEL 1.62% to anyone else, even if they have the same symptoms you have. Selling or giving away this medicine may harm others and is against the law.

ANDROGEL 1.62% is not meant for use in women.

**Who should not use ANDROGEL 1.62%?**

**Do not use ANDROGEL 1.62% if you:**

- have breast cancer
- have or might have prostate cancer
- are pregnant or may become pregnant or are breast-feeding. ANDROGEL 1.62% may harm your unborn or breast-feeding baby.

Women who are pregnant or who may become pregnant should avoid contact with the area of skin where ANDROGEL 1.62% has been applied.

Talk to your healthcare provider before taking this medicine if you have any of the above conditions.

**What should I tell my healthcare provider before using ANDROGEL 1.62%?**

**Before you use ANDROGEL 1.62%, tell your healthcare provider if you:**

- have breast cancer
- have or might have prostate cancer
- have urinary problems due to an enlarged prostate
- have heart problems
- have kidney or liver problems

- have problems breathing while you sleep (sleep apnea)
- have any other medical conditions

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Using ANDROGEL 1.62% with certain other medicines can affect each other.

Especially, tell your healthcare provider if you take:

- insulin
- medicines that decrease blood clotting
- corticosteroids

Know the medicines you take. Ask your healthcare provider or pharmacist for a list of all of your medicines, if you are not sure. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

### **How should I use ANDROGEL 1.62%?**

- It is important that you apply ANDROGEL 1.62% exactly as your healthcare provider tells you to.
- Your healthcare provider will tell you how much ANDROGEL 1.62% to apply and when to apply it.
- Your healthcare provider may change your ANDROGEL 1.62% dose. **Do not** change your ANDROGEL 1.62% dose without talking to your healthcare provider.
- **ANDROGEL 1.62% is to be applied to the area of your shoulders and upper arms that will be covered by a short sleeve t-shirt. Do not** apply ANDROGEL 1.62% to any other parts of your body such as your stomach area (abdomen), penis, or scrotum.
- Apply ANDROGEL 1.62% at the same time each morning. ANDROGEL 1.62% should be applied after showering or bathing.
- **Wash your hands right away** with soap and water after applying ANDROGEL 1.62%.
- Avoid showering, swimming or bathing for at least 2 hours after you apply ANDROGEL 1.62%.
- ANDROGEL 1.62% is flammable until dry. Let ANDROGEL 1.62% dry before smoking or going near an open flame.
- Let the application site dry completely before putting on a t-shirt.

### **Applying ANDROGEL 1.62%:**

**ANDROGEL 1.62% comes in a pump or in packets.**

- **Before applying ANDROGEL 1.62% make sure that your shoulders and upper arms are clean, dry, and that there is no broken skin.**
- The application sites for ANDROGEL 1.62% are the upper arms and shoulders that will be covered by a short sleeve t-shirt (See Figure A).



(Figure A)

**If you are using ANDROGEL 1.62% pump:**

- Before using a new bottle of ANDROGEL 1.62 % for the first time, you will need to prime the pump. To prime the ANDROGEL 1.62% pump, slowly push the pump all the way down 3 times. **Do not** use any ANDROGEL 1.62% that came out while priming. Wash it down the sink to avoid accidental exposure to others. Your ANDROGEL 1.62% pump is now ready to use.
- Remove the cap from the pump. Then, position the nozzle over the palm of your hand and slowly push the pump all the way down. Apply ANDROGEL 1.62% to the application site. You may also apply ANDROGEL 1.62% directly to the application site.
- **Wash your hands with soap and water right away.**

Find Your Dose as Prescribed by Your Healthcare Provider		Application Method
1 PUMP DEPRESSION	20.25 mg	Apply 1 pump depression of ANDROGEL 1.62% to 1 upper arm and shoulder.
2 PUMP DEPRESSIONS	40.5 mg	Apply 1 pump depression of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply 1 pump depression of ANDROGEL 1.62% to the opposite upper arm and shoulder.
3 PUMP DEPRESSIONS	60.75 mg	Apply 2 pump depressions of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply 1 pump depression of ANDROGEL 1.62% to the opposite upper arm and shoulder.
4 PUMP DEPRESSIONS	81 mg	Apply 2 pump depressions of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply 2 pump depressions of ANDROGEL 1.62% to the opposite upper arm and shoulder.

**If you are using ANDROGEL 1.62% packets:**

- Tear open the packet completely at the dotted line. Squeeze from the bottom of the packet to the top.
- Squeeze all of the ANDROGEL 1.62% out of the packet into the palm of your hand. Apply ANDROGEL 1.62% to the application site. You may also apply ANDROGEL 1.62% directly to the application site.
- ANDROGEL 1.62% should be applied right away.
- **Wash your hands with soap and water right away.**

Find Your Dose as Prescribed by Your Healthcare Provider		Application Method
One 20.25 mg packet	20.25 mg	Apply 1 packet of ANDROGEL 1.62% to 1 upper arm and shoulder.
One 40.5 mg packet	40.5 mg	Apply half of the 40.5 mg packet of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply the remaining packet contents to the opposite upper arm and shoulder.
One 40.5 mg packet and one 20.25 mg packet	60.75 mg	Apply one 40.5 mg packet of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply one 20.25 mg packet of ANDROGEL 1.62% to the opposite upper arm and shoulder.
Two 40.5 mg packets	81 mg	Apply one 40.5 mg packet of ANDROGEL 1.62% to 1 upper arm and shoulder and then apply one 40.5 mg packet of ANDROGEL 1.62% to the opposite upper arm and shoulder.

**What are the possible side effects of ANDROGEL 1.62%?**

**See “What is the most important information I should know about ANDROGEL 1.62%?”**

**ANDROGEL 1.62% can cause serious side effects including:**

- **If you already have enlargement of your prostate gland your signs and symptoms can get worse while using ANDROGEL 1.62%.** This can include:
  - increased urination at night
  - trouble starting your urine stream
  - having to pass urine many times during the day
  - having an urge that you have to go to the bathroom right away
  - having a urine accident
  - being unable to pass urine or weak urine flow
- **Possible increased risk of prostate cancer.** Your healthcare provider should check you for prostate cancer or any other prostate problems before you start and while you use ANDROGEL 1.62%.
- **In large doses ANDROGEL 1.62% may lower your sperm count.**
- **Swelling of your ankles, feet, or body, with or without heart failure.**
- **Enlarged or painful breasts.**
- **Have problems breathing while you sleep (sleep apnea).**
- **Blood clots in the legs.** This can include pain, swelling, or redness of your legs.

**Call your healthcare provider right away if you have any of the serious side effects listed above.**

**The most common side effects of ANDROGEL 1.62% include:**

- increased prostate specific antigen (a test used to screen for prostate cancer)
- mood swings
- hypertension
- increased red blood cell count
- skin irritation where ANDROGEL 1.62% is applied

**Other side effects include** more erections than are normal for you or erections that last a long time.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of ANDROGEL 1.62%. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store ANDROGEL 1.62%?**

- Store ANDROGEL 1.62% at 59°F to 86°F (15°C to 30°C).
- When it is time to throw away the pump or packets, safely throw away used ANDROGEL 1.62% in household trash. Be careful to prevent accidental exposure of children or pets.
- Keep ANDROGEL 1.62% away from fire.

**Keep ANDROGEL 1.62% and all medicines out of the reach of children.**

**General information about the safe and effective use of ANDROGEL 1.62%**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ANDROGEL 1.62% for a condition for which it was not prescribed. Do not give ANDROGEL 1.62% to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about ANDROGEL 1.62%. If you would like more information, talk to your healthcare provider. You can ask your pharmacist or healthcare provider for information about ANDROGEL 1.62% that is written for health professionals.

For more information, go to [www.androgel.com](http://www.androgel.com) or call 1-800-241-1643.

**What are the ingredients in ANDROGEL 1.62%?**

**Active ingredient:** testosterone

**Inactive ingredients:** carbopol 980, ethyl alcohol, isopropyl myristate, purified water and sodium hydroxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

A090630053786 September 2012

© 2012 Abbott Laboratories

Marketed by:

Abbott Laboratories

North Chicago, IL, 60064, U.S.A.

## PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 54569-6337-0

Dispense the accompanying Medication Guide to each patient.

AndroGel® (testosterone gel) 1.62% CIII

20.25 mg of testosterone per pump actuation\*

\*Each actuation delivers 1.25 g of gel

For Topical Use Only

Rx only

Multi-dose pump capable of dispensing 60 metered pump actuations.

A-S Medication Solutions

NDC 0051-8462-33  
[Solvay Pharmaceuticals]  
Product No. 6337-0  
LOT 9999999

**ANDROGEL**  
**1.62 %**

EACH PUMP ACTUATION CONTAINS:  
TESTOSTERONE 20.25 MG  
EACH PUMP ACTUATION DELIVERS  
1.25 GM OF GEL  
STORE AT 77 DEGREES F; EXCURSIONS  
PERMITTED TO 59-86 DEGREES F

**75 GM PUMP**

Distributed By  
**A-S MEDICATION SOLUTIONS**  
**WWW.A-SMEDS.COM**  
Libertyville, IL 60040  
Mfg: Solvay Pharmaceuticals  
Marietta, GA  
**RX ONLY - RX# CX748288**  
Dosage: See Package Insert  
**DISCARD AFTER: 12/45**

**ANDROGEL**  
**1.62 %**  
**75 GM PUMP**

NDC 0051-8462-33  
RX CX748288  
PROD 6337-0  
LOT 9999999  
EXP 12/45

**PATIENT INSTRUCTIONS**

**KEEP MEDICATION OUT OF THE REACH OF CHILDREN**

**APPLY \_\_\_\_\_ PUMP ACTUATION(S) ONCE DAILY IN THE  
MORNING AS DIRECTED.**

**READ MEDICATION GUIDE BEFORE STARTING AND WITH EACH REFILL.  
WASH HANDS IMMEDIATELY WITH SOAP AND WATER AFTER APPLICATION.  
AVOID FIRE, FLAME, OR SMOKING UNTIL THE GEL HAS DRIED.  
AVOID EXPOSURE TO WOMEN AND CHILDREN TO ANDROGEL AND TO UNWASHED OR  
UNCLOTHED APPLICATION SITES.**

Federal Law prohibits transfer of this drug to any person other than the patient for whom it was prescribed.

## ANDROGEL

testosterone gel

### Product Information

Product Type

HUMAN  
PRESCRIPTION DRUG

Item Code (Source)

NDC:54569-  
6337(NDC:0051-8462)



<b>Route of Administration</b>	TRANSDERMAL	<b>DEA Schedule</b>	CIII
--------------------------------	-------------	---------------------	------

  

<b>Active Ingredient/Active Moiety</b>		
<b>Ingredient Name</b>	<b>Basis of Strength</b>	<b>Strength</b>
testosterone (UNII: 3XMK78S47O) (testosterone - UNII:3XMK78S47O)	testosterone	16.2 mg in 1 g

  

<b>Inactive Ingredients</b>	
<b>Ingredient Name</b>	<b>Strength</b>
carbomer homopolymer type C (UNII: 4Q93RCW27E)	
alcohol (UNII: 3K9958V90M)	
isopropyl myristate (UNII: 0RE8K4LNJS)	
water (UNII: 059QF0KO0R)	
sodium hydroxide (UNII: 55X04QC32I)	

  

<b>Packaging</b>				
<b>#</b>	<b>Item Code</b>	<b>Package Description</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
1	NDC:54569-6337-0	75 g in 1 BOTTLE, PUMP		

  

<b>Marketing Information</b>			
<b>Marketing Category</b>	<b>Application Number or Monograph Citation</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
NDA	NDA022309	04/29/2011	

**Labeler** - A-S Medication Solutions LLC (830016429)

<b>Establishment</b>			
<b>Name</b>	<b>Address</b>	<b>ID/FEI</b>	<b>Business Operations</b>
A-S Medication Solutions LLC		830016429	relabel(54569-6337)